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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,852	12/10/2003	Frederick L. Hall	06666-042002 / 2895	4628

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EXAMINER	
DEBERRY, REGINA M	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 06/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,852	HALL ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-69 and 72-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-69 and 72-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 07 April 2006 has been entered in full. Claims 70 and 71 are cancelled. Claims 66-69 and 72-80 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection to claims 66-71 under 35 U.S.C. 102(e) as being anticipated by Hall *et al.,* US Patent 6,387,663 B1, as set forth at pages 2-3 of the previous Office Action (07 December 2005), is *withdrawn* in view of the amendment (07 April 2006).

The rejection to claims 72-79 under 35 U.S.C. 102(e) as being anticipated by Hall *et al.,* US Patent 6,955,898 B2, as set forth at page 3 of the previous Office Action (07 December 2005), is *withdrawn* in view of the amendment (07 April 2006).

The rejection to claims 66, 67, 70, 72-74, 76-78 and 80 under 35 U.S.C. 102(b) as being anticipated by Hall *et al.,* WO 96/39430, as set forth at page 4 of the previous Office Action (07 December 2005), is *withdrawn* in view of the amendment (07 April 2006).

The rejection to claims 66, 67, 70-74, 76-78 and 80 under 35 U.S.C. 102(b) as being anticipated by Nishi *et al.,* Proc. Natl. Acad. Sci. USA, Vol. 95:7018-7023 (1998), as set forth at page 4 of the previous Office Action (07 December 2005), is *withdrawn* in view of the amendment (07 April 2006).

The rejection to claims 66-69, 71-74, 76-78 under 35 U.S.C. 102(b) as being anticipated by Gordon *et al.,* Human Gene Therapy Vol. 8:1385-1394 (1997), as set forth at page 5 of the previous Office Action (07 December 2005), is *withdrawn* in view of the amendment (07 April 2006).

The rejection to claims 75 and 79 under 35 U.S.C. 103(a) as being unpatentable over by Gordon *et al.,* Human Gene Therapy Vol. 8:1385-1394 (1997) in view of Temin *et al.,* US Patent No. 4,980,289, as set forth at pages 5-6 of the previous Office Action (07 December 2005), is *withdrawn* in view of the amendment (07 April 2006).

The rejection to claims 66-71 under 35 U.S.C. 101 (double patenting rejection) as claiming the same invention as that of claims 1-4, of U.S. Patent No. 6,387,663 B1, as set forth at pages 6-7 of the previous Office Action (07 December 2005), is *withdrawn* in view of the amendment (07 April 2006).

The rejection to claims 72-79 are under 35 U.S.C. 101 (double patenting rejection) as claiming the same invention as that of claims 1-8, 11, of U.S. Patent No. 6,955,898 B2, as set forth at page 8 of the previous Office Action (07 December 2005), is *withdrawn* in view of the amendment (07 April 2006).

NEW REJECTIONS:

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 66-69 and 72-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 66, 72, 80 recite the broad recitation "hemopoietic growth factors" and the claims also recite "stem cell factor (SCF) and erythropoietin (EPO)" which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

Claims 66-69 and 72-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a fusion polypeptide (nucleic acid sequence encoding a fusion polypeptide or a pharmaceutical composition comprising a fusion polypeptide) comprising a collagen-binding domain and an epithelial cell proliferation-modulation agent, wherein the epithelial cell proliferation-modulating agent is a hemopoietic growth factor (HeGFs), nerve growth factor (NGF) or erythropoietin (EPO),

does not reasonably provide enablement for:

a fusion polypeptide (nucleic acid sequence encoding a fusion polypeptide or a pharmaceutical composition comprising a fusion polypeptide) comprising neu, inhibin α, inhibin β, Mullerian inhibitory substance, wnt, hst/ks3, stem cell factor, leukemia inhibitory factor or any of the recited receptors.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the following reasons. Growth factors would possess the epithelial cell proliferation modulating activity not the receptors. Furthermore, the instant specification teaches the epithelial cell proliferation-modulating agent as a growth factor *not a growth factor receptor* (see specification, page 10, lines 18-20 and original claims 5 and 6). Newly amended claims 66, 72 and 80 recite various receptors. In addition, the instant claims recite Mullerian inhibitory substance, inhibin α, inhibin β, wnt-2, hst/ks3, stem cell factor and leukemia inhibitory factor as proteins with epithelial cell proliferation-modulating activity. The specification only demonstrates epidermal growth factor (EGF) as a protein with epithelial cell proliferation activity. The examples teach the construction of a fusion protein comprising a collagen binding

domain and EGF. The examples demonstrate that the fusion protein promotes epithelial cell growth in wound healing. The instant examples and the art of record fail to teach that any of the recited proteins (Mullerian inhibitory substance, inhibin α, inhibin β, wnt-2, hst/ks3, stem cell factor and leukemia inhibitory factor) affect epithelial cell growth and/or differentiation.

Due to the large quantity of experimentation necessary to use the claimed factors and receptors other than as a polypeptide having the activity of epithelial cell proliferation-modulating activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which fails to teach that the claimed factors and receptors have epithelial cell proliferation-modulating activity and the unpredictability of what other activities the claimed factors and receptors may have on epithelial cell proliferation-modulating activity, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claim Rejections - 35 USC § 103(a)

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 72-79 are rejected under 35 U.S.C. 103(a) as being obvious over Hall *et al.,* U.S. Patent No. 6,955,898 B2 in view of Carlini *et al.,* Kidney International Vol. 55 pages 546-553, 1999.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The instant claims are drawn to a nucleic acid sequence encoding a fusion polypeptide comprising a collagen-binding domain and an epithelial cell proliferation-modulating agent, wherein the epithelial cell proliferation-modulating agent includes

erythropoietin (EPO). The instant claims are also drawn to a promotor, expression vector, host cell and a method of making the fusion protein.

Hall *et al.* teach an isolated nucleic acid encoding a fusion polypeptide, wherein said fusion polypeptide comprises a collagen-binding domain which binds exposed vascular collagen and an angiogenesis modulating domain, wherein said angiogenesis modulating domain directly effects endothelial cell proliferation. Hall *et al.* teach a promotor, expression vector, host cell and a method of producing the fusion protein (claims). Hall *et al.* do not teach that EPO has endothelial cell growth activity. Carlini *et al.* teach that EPO induces endothelial cell growth (abstract and page 552).

It would have been obvious to one of skill in the art at the time the invention was made to modify the isolated nucleic acid encoding a fusion polypeptide, wherein said fusion polypeptide comprises a collagen-binding domain and an angiogenesis modulating domain, which directly effects endothelial cell proliferation as taught by Hall *et al.* by using the endothelial cell proliferating EPO protein as taught by Carlini *et al.* with a reasonable expectation of success. The motivation and expected success is provided by Carlini *et al.,* who teach that EPO acts as a survival factor increasing the viability of injured endothelial cells. A fusion protein comprising a collagen binding domain and EPO can be used to specifically target EPO to damaged endothelium. Furthermore, the genus of an angiogenesis modulating domain, which directly effects endothelial cell proliferation renders the species of EPO (which promotes endothelial cell proliferation) obvious.

Claims 66, 68 and 69 are rejected under 35 U.S.C. 103(a) as being obvious over Hall *et al.,* U.S. Patent No. 6,387,663 B1 in view of Carlini *et al.,* Kidney International Vol. 55 pages 546-553, 1999.

The instant claims 66, 68 and 69 are drawn to a fusion polypeptide comprising a collagen-binding domain and an epithelial cell proliferation-modulating agent, wherein the epithelial cell proliferation-modulating agent includes erythropoietin (EPO). The claims are also drawn to a collagen-binding domain of von Willebrand factor and SEQ ID NO:1.

Hall *et al.* teach a fusion polypeptide comprising a collagen-binding domain which binds exposed vascular collagen and an angiogenesis modulating domain, wherein said angiogenesis modulating domain directly effects endothelial cell proliferation. Hall *et al.* teach a collagen-binding domain of von Willebrand factor and SEQ ID NO:1. Hall *et al.* do not teach that EPO has endothelial cell growth activity. Carlini *et al.* teach that EPO induces endothelial cell growth (abstract and page 552).

It would have been obvious to one of skill in the art at the time the invention was made to modify a fusion polypeptide comprising a collagen-binding domain and an angiogenesis modulating domain, which directly effects endothelial cell proliferation as taught by Hall *et al.* by using the endothelial cell proliferating EPO protein as taught by Carlini *et al.* with a reasonable expectation of success. The motivation and expected success is provided by Carlini *et al.,* who teach that EPO acts as a survival factor increasing the viability of injured endothelial cells. A fusion protein comprising a collagen-binding domain and EPO can be used to specifically target EPO to damaged

endothelium. Furthermore, the genus of an angiogenesis modulating domain, which directly effects endothelial cell proliferation renders the species of EPO (which promotes endothelial cell proliferation) obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 72-79 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,955,898 B2 in view of Carlini *et al.,* Kidney International Vol. 55 pages 546-553, 1999. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of U.S. Patent No. 6,955,898 B2 are drawn to an isolated nucleic acid encoding a fusion polypeptide, wherein said fusion polypeptide comprises a collagen-

binding domain which binds exposed vascular collagen and an angiogenesis modulating domain, wherein said angiogenesis modulating domain directly effects endothelial cell proliferation. The claims of U.S. Patent No. 6,955,898 B2 are also drawn to a promotor, expression vector, host cell and a method of producing the fusion protein.

Claims 72-79 of the instant application are drawn to a nucleic acid sequence encoding a fusion polypeptide comprising a collagen-binding domain and an epithelial cell proliferation-modulating agent, wherein the epithelial cell proliferation-modulating agent includes erythropoietin (EPO). Claims 73-79 are drawn to a promotor, expression vector, host cell and a method of making the fusion protein. Claims 72-79 do not recite that EPO has endothelial cell growth activity. Carlini *et al.* teach that EPO induces endothelial cell growth.

It would have been obvious to one of skill in the art at the time the invention was made to modify the isolated nucleic acid encoding a fusion polypeptide, wherein said fusion polypeptide comprises a collagen-binding domain and an angiogenesis modulating domain, which directly effects endothelial cell proliferation as taught in claims 1-8 of U.S. Patent No. 6,955,898 B2 by using the endothelial cell proliferating EPO protein as taught by Carlini *et al.* with a reasonable expectation of success. The motivation and expected success is provided by Carlini *et al.,* who teach that EPO acts as a survival factor increasing the viability of injured endothelial cells. A fusion protein comprising a collagen binding domain and EPO can be used to specifically target EPO to damaged endothelium. Furthermore, the genus of an angiogenesis modulating

domain, which directly effects endothelial cell proliferation renders the species of EPO (which promotes endothelial cell proliferation) obvious.

Claims 66, 68 and 69 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,387,663 B1 in view of Carlini *et al.,* Kidney International Vol. 55 pages 546-553, 1999. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of U.S. Patent No. 6,387,663 B1 are drawn to a fusion polypeptide comprising a collagen-binding domain which binds exposed vascular collagen and an angiogenesis modulating domain, wherein said angiogenesis modulating domain directly effects endothelial cell proliferation. The claims of U.S. Patent No. 6,387,663 are also drawn to a collagen-binding domain of von Willebrand factor and SEQ ID NO:1.

Claims 66, 68 and 69 of the instant application are drawn to a fusion polypeptide comprising a collagen-binding domain and an epithelial cell proliferation-modulating agent, wherein the epithelial cell proliferation-modulating agent includes erythropoietin (EPO). Claims 68 and 69 are drawn to a collagen-binding domain of von Willebrand factor and SEQ ID NO:1. Claims 66, 68 and 69 do not recite that EPO has endothelial cell growth activity. Carlini *et al.* teach that EPO induces endothelial cell growth.

It would have been obvious to one of skill in the art at the time the invention was made to modify a fusion polypeptide comprising a collagen binding domain and an angiogenesis modulating domain, which directly effects endothelial cell proliferation as

taught in claims 1-3 of U.S. Patent No. 6,387,663 B1 by using the endothelial cell proliferating EPO protein as taught by Carlini *et al.* with a reasonable expectation of success. The motivation and expected success is provided by Carlini *et al.,* who teach that EPO acts as a survival factor increasing the viability of injured endothelial cells. A fusion protein comprising a collagen-binding and EPO can be used to specifically target EPO to damaged endothelium. Furthermore, the genus of an angiogenesis modulating domain, which directly effects endothelial cell proliferation, renders the species of EPO (which promotes endothelial cell proliferation) obvious.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RMD
6/14/06

Marianne P. Allen 6/19/06
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